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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,491	02/13/2001	Dallas L. Clouatre	71286.010110	8229

48329 7590 02/24/2005

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EXAMINER	
JONES, DWAYNE C	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/781,491	CLOUATRE ET AL.	
	Examiner	Art Unit	
	Dwayne C. Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 25, 2004 and December 2, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s)_____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-18 are pending.

2. Claims 1-18 are rejected.

Response to Arguments

3. Applicants' arguments, see in particular the Declaration under 37 C.F.R. 1.131(A), filed May 25, 2004, with respect to the rejection(s)of claim(s) 1-18 under 35 U.S.C. 102(e) and 35 U.S.C. 103(a), mainly for the reference of Shrivastava et al. of U.S. Patent No. 6,221,901 B1 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Sullivan et al. in view of Hardman of Goodman and Gilman's THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 9th Edition, and view of DiPiro of PHARMACOTHERAPY, A Pathophysiologic Approach and in further view of Solomons and McMurry.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1 and 4-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan et al. in view of Hardman of Goodman and Gilman's THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 9th Edition, and view of DiPiro of PHARMACOTHERAPY, A Pathophysiologic Approach and in further view of the prior art teachings of Solomons and McMurry.

8. Sullivan et al. disclose of treating obesity with the administration of hydroxycitrate, such as sodium hydroxycitrate, (see abstract and page 768, column 2, 1st paragraph). Sullivan et al. also teach that because hydroxycitrate is a known

inhibitor of ATP citrate lyase, its administration inhibited significantly in vivo rates of fatty acid and cholesterol synthesis, (see page 767, column 2 and pages 774-775). Sullivan et al. disclose that the in vivo models of obese rats had reduced food intake and body weight gain with the administration of hydroxycitrate. The prior art reference of Hardman of Goodman and Gilman's THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 9th Edition teach that obesity and hypertension are closely associated, and the degree of obesity is positively correlated with the incidence of hypertension, (see page 804, column 1, under the section entitled "Reduction of Body Weight").

9. Next, the prior art reference is used to show inter alia that the treatment plan for hypertension should always include measures to minimize contributing factors and to reduce other risks. For example, aggressive dietary programs have been shown to reduce cardiovascular events in high-risk groups. In addition, DiPiro et al. specifically disclose that hypertensive patients screened for a Muliple Risk Factor Intervention Trial study, those with a modest degree of cholesterol elevation, around 245 mg/dL, were found to have three to four times the relative risk of coronary heart disease of those with a total cholesterol level below 183 mg/dl, (see page 101, under the section entitled "Treatment (See Addendum)").

10. Moreover, it is well within the level of the skilled artisan to convert between acid and its conjugate base, for instance (-) hydroxycitric acid and (-) hydroxycitrate. Sullivan et al. teach of the therapeutic administration of (-) hydroxycitrate to treat obesity, (see column 2, lines 34-48). Sullivan et al. is silent to the lactone form of the (-)

hydroxycitrate, it is widely accepted in the art that the cyclization of 5-membered ring into a lactone from its acyclic acid chain occurs readily. In fact, carboxylic acids whose molecules have a hydroxyl group on a gamma- or delta- carbon atom undergo an intramolecular esterification to give cyclic esters known as gamma- or delta- lactones, (see page 799 of Solomons, Organic Chemistry 3rd Edition). It is also known in the art that carboxylic acid can be readily converted into other carboxylic acid derivates, such as carboxylic acid esters and amides, (see McMurry of Organic Chemistry, 2nd Edition, pages 759-767). It is also within the purview of the skilled artisan to simply convert an acidic group of an active agent, for instance (-) hydroxycitrate, into its corresponding ester and/or amide derivatives for the purpose of generating controlled-release forms of the active agent because these derivatives have the extra step of either removing the ester or amide groups before the active agent can be utilized. Although the prior art reference of Sullivan et al. teaches of using the sodium salt of hydroxycitrate it is well within the level of skill of the artisan to substitute one pharmaceutically acceptable cation for another. The determination of a dosage having the optimum therapeutic index, which includes pharmaceutically acceptable salts, is well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug while minimizing adverse and/or unwanted side-effects. Accordingly, these references make obvious the instantly claimed subject matter.

11. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan et al. in view of Hardman of Goodman and Gilman's THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 9th Edition, and view of DiPiro of PHARMACOTHERAPY, A Pathophysiologic Approach and in further view of the prior art teachings of Solomons and McMurry.

12. Sullivan et al. disclose of treating obesity with the administration of hydroxycitrate, such as sodium hydroxycitrate, (see abstract and page 768, column 2, 1st paragraph). Sullivan et al. also teach that because hydroxycitrate is a known inhibitor of ATP citrate lyase, its administration inhibited significantly in vivo rates of fatty acid and cholesterol synthesis, (see page 767, column 2 and pages 774-775). Sullivan et al. disclose that the in vivo models of obese rats had reduced food intake and body weight gain with the administration of hydroxycitrate. The prior art reference of Hardman of Goodman and Gilman's THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, 9th Edition teach that obesity and hypertension are closely associated, and the degree of obesity is positively correlated with the incidence of hypertension, (see page 804, column 1, under the section entitled "Reduction of Body Weight").

13. Next, the prior art reference is used to show inter alia that the treatment plan for hypertension should always include measures to minimize contributing factors and to reduce other risks. For example, aggressive dietary programs have been shown to reduce cardiovascular events in high-risk groups. In addition, DiPiro et al. specifically disclose that hypertensive patients screened for a Muliple Risk Factor Intervention Trial

study, those with a modest degree of cholesterol elevation, around 245 mg/dL, were found to have three to four times the relative risk of coronary heart disease of those with a total cholesterol level below 183 mg/dl, (see page 101, under the section entitled "Treatment (See Addendum)").

14. Moreover, DiPiro et al. teach that body weight and obesity are common characteristics in diabetes. DiPiro et al. also teach of various causes of diabetes, inter alia, elevated insulin and glucocorticoids and hormones, (see Table 54.1 on page 806 and pages 805-811). Accordingly, by treating hypertension as well as obesity with the administration of (-) hydroxycitrate or an analog thereof to an individual in need thereof, the individual would also be treating diabetes by inter alia, controlling the weight of the individual and also by lowering glucose levels as well as insulin and other hormones, see DiPiro et al. Furthermore, the courts have held, *In re Swinehart*, 169 USPQ 226, "a newly discovered property does not necessarily mean that the product is unobvious, since this property may be inherent in the prior art." In view of this case law, applicants' recitation of lowering elevated insulin and elevated glucocorticoid levels is an inherent process that already occurs with the administration of the (-)-hydroxycitrate to treat obesity and hypertension in the prior art references of Sullivan et al. in view of Hardman.

15. In addition, it would have been obvious to the skilled artisan to utilize analogs of (-)-hydroxycitrate, such as (-)-hydroxycitric acid, to treat hypertension. Moreover, the lowering of insulin and glucocorticoid levels is just an inherent biochemical mechanism that already occurs with the administration of (-)-hydroxycitrate as well as its analogs.

Clearly, it would have been obvious, if not inherent, to the skilled artisan that by treating an individual with (-) hydroxycitrate, glucose, insulin and other hormone levels could be modified and manipulated especially since it is known in the art that obesity is related to diabetes and that a composition containing (-) hydroxycitrate is known to treat obesity.

16. Moreover, it is well within the level of the skilled artisan to convert between acid and its conjugate base, for instance (-) hydroxycitric acid and (-) hydroxycitrate. Sullivan et al. teach of the therapeutic administration of (-) hydroxycitrate to treat obesity, (see column 2, lines 34-48). Sullivan et al. is silent to the lactone form of the (-) hydroxycitrate, it is widely accepted in the art that the cyclization of 5-membered ring into a lactone from its acyclic acid chain occurs readily. In fact, carboxylic acids whose molecules have a hydroxyl group on a gamma- or delta- carbon atom undergo an intramolecular esterification to give cyclic esters known as gamma- or delta- lactones, (see page 799 of Solomons, Organic Chemistry 3rd Edition). It is also known in the art that carboxylic acid can be readily converted into other carboxylic acid derivates, such as carboxylic acid esters and amides, (see McMurry of Organic Chemistry, 2nd Edition, pages 759-767). It is also within the purview of the skilled artisan to simply convert an acidic group of an active agent, for instance (-) hydroxycitrate, into its corresponding ester and/or amide derivatives for the purpose of generating controlled-release forms of the active agent because these derivatives have the extra step of either removing the ester or amide groups before the active agent can be utilized. Although the prior art reference of Sullivan et al. teaches of using the sodium salt of hydroxycitrate it is well within the level of skill of the artisan to substitute one pharmaceutically acceptable

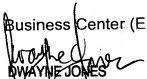
cation for another. The determination of a dosage having the optimum therapeutic index, which includes pharmaceutically acceptable salts, is well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug while minimizing adverse and/or unwanted side-effects. Accordingly, these references make obvious the instantly claimed subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Wednesdays, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (571)-273-8300.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see http://pair-direct.uspto.gov. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 1-866-217-9197 (toll free).



SWAYNE JONES
PRIMARY EXAMINER
Tech. Ctr. 1614
February 21, 2005